# UNITED STATES DISTRICT COURT FOR THE NORTHERN DISTRICT OF OHIO EASTERN DIVISION

IN RE NATIONAL PRESCRIPTION OPIATE LITIGATION

MDL No. 2804 Case No. 17-md-2804 Judge Dan Aaron Polster

This document relates to:

Track Three Cases

DECLARATION OF STEVEN N. HERMAN IN SUPPORT OF THE PHARMACY DEFENDANTS' MOTION TO EXCLUDE CERTAIN OPINIONS AND TESTIMONY OF DR. KATHERINE KEYES

EXHIBIT 26

## **Original Investigation**

# The Changing Face of Heroin Use in the United States A Retrospective Analysis of the Past 50 Years

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**IMPORTANCE** Over the past several years, there have been a number of mainstream media reports that the abuse of heroin has migrated from low-income urban areas with large minority populations to more affluent suburban and rural areas with primarily white populations.

**OBJECTIVE** To examine the veracity of these anecdotal reports and define the relationship between the abuse of prescription opioids and the abuse of heroin.

**DESIGN, SETTING, AND PARTICIPANTS** Using a mixed-methods approach, we analyzed (1) data from an ongoing study that uses structured, self-administered surveys to gather retrospective data on past drug use patterns among patients entering substance abuse treatment programs across the country who received a primary (*DSM-IV*) diagnosis of heroin use/dependence (n = 2797) and (2) data from unstructured qualitative interviews with a subset of patients (n = 54) who completed the structured interview.

MAIN OUTCOMES AND MEASURES In addition to data on population demographics and current residential location, we used cross-tabulations to assess prevalence rates as a function of the decade of the initiation of abuse for (1) first opioid used (prescription opioid or heroin), (2) sex, (3) race/ethnicity, and (4) age at first use. Respondents indicated in an open-ended format why they chose heroin as their primary drug and the interrelationship between their use of heroin and their use of prescription opioids.

RESULTS Approximately 85% of treatment-seeking patients approached to complete the Survey of Key Informants' Patients Program did so. Respondents who began using heroin in the 1960s were predominantly young men (82.8%; mean age, 16.5 years) whose first opioid of abuse was heroin (80%). However, more recent users were older (mean age, 22.9 years) men and women living in less urban areas (75.2%) who were introduced to opioids through prescription drugs (75.0%). Whites and nonwhites were equally represented in those initiating use prior to the 1980s, but nearly 90% of respondents who began use in the last decade were white. Although the "high" produced by heroin was described as a significant factor in its selection, it was often used because it was more readily accessible and much less expensive than prescription opioids.

**CONCLUSION AND RELEVANCE** Our data show that the demographic composition of heroin users entering treatment has shifted over the last 50 years such that heroin use has changed from an inner-city, minority-centered problem to one that has a more widespread geographical distribution, involving primarily white men and women in their late 20s living outside of large urban areas.

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CME Quiz at jamanetworkcme.com and CME Questions page 844

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n recent years, there have been a number of mainstream media reports that the abuse of heroin has migrated from low-income urban areas with large minority populations to more affluent suburban and rural areas with primarily white populations. <sup>1-8</sup> Large-scale epidemiological studies have documented significant increases in heroin use<sup>9,10</sup> and overdose-related hospitalizations<sup>9,11</sup> nationwide, particularly over the past 10 years, but there have been few systematic studies on the demographics of today's heroin users compared with those who used heroin 40 to 50 years ago who were primarily young men from minority groups living in urban areas. <sup>12-19</sup>

Part of this increase in heroin use and apparent migration to a new class of users appears to be due to the coincidental increase in the abuse of prescription opioids over the last 20 years, 11,12,20-23 arguably accelerated by the release of OxyContin in the mid-1990s, 24,25 which made large quantities of oxycodone hydrochloride readily available for inhalation and intravenous injection. Given that prescription opioids are legal, are prescribed by a physician, and are thus considered trustworthy and predictable (eg, the dose is clearly specified on a distinctive tablet or pill), many users viewed these drugs as safer to use than other illicit substances.<sup>26,27</sup> However, there is now growing evidence that some prescription opioid abusers, particularly those who inhale or inject their drugs, graduate or shift to heroin, 12,21,24,25,28-33 at least in part because it has become more accessible and far less expensive than prescription opioids. 12,28,33-37 Thus, one could assume that more recent users of heroin would share more demographic features with today's prescription opioid abusers than with those individuals who initiated their heroin use 40 to 50 years ago.

To assess this postulate, we used a mixed-methods approach, analyzing data from (1) an ongoing study using structured, self-administered surveys to gather retrospective data on drug use patterns among patients entering substance abuse treatment programs across the country who received a primary (DSM-IV) diagnosis of heroin use/dependence (n = 2797) and from (2) unstructured qualitative interviews with a subset of patients (n = 54) who completed the structured interview.

## Methods

#### Study Sample

Our study used data from the ongoing nationwide Survey of Key Informants' Patients (SKIP) Program, a key element of the postmarketing Researched Abuse, Diversion and Addiction-Related Surveillance (RADARS) System.<sup>38</sup> The SKIP Program consists of more than 150 publicly and privately funded treatment centers (key informants), balanced geographically with coverage in 48 states, that recruit patients/clients to complete an anonymous survey. Participants must be 18 years of age or older and must meet *DSM-IV* criteria for substance abuse with a primary drug that is an opioid (prescription drug or heroin). Approximately 85% of patients approached by treatment center staff agreed to complete the survey, which was identified by a unique case number and sent directly to Wash-

ington University in St Louis, Missouri, by the respondent. Participants were compensated with a \$20 Walmart gift card. The SKIP data were analyzed from third quarter 2010 to third quarter 2013. Of 9346 opioid-dependent patients who completed the survey in that time frame, 2797 self-reported heroin as their primary drug of abuse (eg, the drug used most frequently in the month prior to treatment), the focus of the present analysis.

To supplement and add context to the structured survey in the SKIP Program, a subset of patients indicated (by mailing in a postcard provided with the survey) that they were willing to give up their anonymity and participate in an unstructured interview-based study, which was named the Researchers and Participants Interacting Directly (RAPID) program. Based on the reflexive nature of qualitative research, the purpose of this program is to develop a 2-way exchange of information with participants through brief, periodic webbased interviews, where questions can be developed, administered, and answered within a short time period to establish real-time data. The collection period for this RAPID interview was during the fourth quarter of 2013; 165 treatment clients consented to participate in the study during this 3-month period by completing and returning the anonymous survey, with 54 of these clients indicating heroin as their a primary drug of abuse. Participants in the RAPID program were compensated with a \$10 Visa check card. All protocols were approved by the Washington University in St Louis institutional review board.

## **Analyzed SKIP Variables**

#### Substance Abuse

The SKIP respondents were asked to identify (1) the opioid used most frequently in the past month to get high (eg, their primary drug), stratified by opioid compound (eg, fentanyl, heroin, or oxycodone), and (2) how often they abused their primary drug (once a month, 2-4 times a month, once a week, 2-4 times a week, once a day, more than once a day, or more than 5 times a day). Respondents were asked at what age they began abusing opioids regularly (≥2 times per week) and were subsequently asked to specify, in their own words, the first opioid they abused regularly. In addition, respondents were asked to identify (1) all opioid compounds used to get high in the month prior to treatment and (2) pastmonth use of other substances for recreational/nonmedical purposes (tobacco, alcohol more than 4 times in 1 day, marijuana, 3,4-methylenedioxymethamphetamien [MDMA, also known as Ecstasy], cocaine or crack cocaine, methamphetamine [also known as crystal meth], hallucinogens, antianxiety medications, sleep medications, muscle relaxants, or antidepressants).

#### **Demographic Variables**

The survey in the SKIP Program includes the following demographic variables: (1) sex (male or female), (2) age (continuous), (3) race/ethnicity (white, African American, Asian or Pacific Islander, Native American; Latino, or other race), and (4) self-declared area of current residence (large urban, small urban, suburban, or rural).

#### **RAPID Interviews**

The RAPID participants were contacted to complete a self-administered Internet-based questionnaire via SurveyMonkey and, if applicable, participated in follow-up e-mail exchanges to clarify ambiguous responses and expound on answers provided in the questionnaire. Other than demographics, participants were asked about their opioid abuse patterns, and those that indicated both a primary drug of heroin and past or current abuse of prescription opioids were asked to explain, in an open-ended format, why they chose to use heroin more frequently than prescription opioids. In addition, respondents were also asked to identify whether they would prefer to abuse heroin or prescription opioids in a hypothetical world where cost and accessibility would not limit drug selection, and to subsequently explain their preference.

#### **Data Analyses**

To assess time-related changes in the demographic characteristics of heroin users, we calculated the decade of a respondent's first regular opioid abuse using the following formula: (year of survey completion – age at survey completion) + age of first regular opioid abuse = year of first regular opioid abuse. The year of first regular opioid abuse was then categorized by its decade block starting from 1960 (1970, 1980, 1990, 2000, and 2010).

Quantitative data in both SKIP and RAPID data sets were analyzed using IBM SPSS Statistics version 20. The following variables were transformed into binary measures (1/0): (1) first opioid used (prescription opioid/heroin), (2) sex (male/female), (3) race/ethnicity (white/nonwhite), and (4) area of residence (large urban/small urban and nonurban [suburban/rural]). Also, in addition to population demographics, crosstabulations were used to assess prevalence rates as a function of decade of first opioid use.

A review of the open-ended responses using the principles of thematic analysis led to the identification of just 3 primary decision-making factors involved in the selection and exclusion of particular opioids as primary drugs of abuse: (1) ease of accessibility, including monetary costs; (2) personal feelings on the "high" provided by various opioids; and (3) ease of extraction for inhalation and injection. Once these themes had been established, NVivo version 9 (QSR International) was used to code the presence of each theme (yes or no) in each individual response.

## Results

#### **Demographics of SKIP and RAPID Respondents**

Our **Table** summarizes the gross demographic features of those participating in the SKIP (n = 2757) and RAPID (n = 54) programs. As can be seen, the RAPID subset, although much smaller, was quite similar to the larger SKIP sample. The majority of respondents who self-reported a primary drug of heroin were male, white, and in their early 30s at the time of survey completion.

### **Residential Location and Drug Use Patterns**

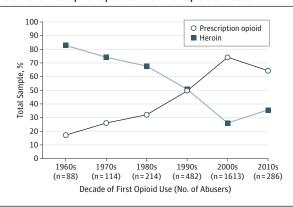
A much greater percentage of heroin users completing the survey in the SKIP Program reported currently living in small ur-

Table. Comparison of SKIP and RAPID Demographic Data

	No. (%) of Respondents	
Characteristic	SKIP (n = 2757)	RAPID (n = 54)
Male sex	1544 (56.0)	32 (58.5)
Age, mean (SEM), y	32.7 (0.2)	34.8 (1.5)
Race/ethnicity		
White	2192 (79.5)	45 (83.3)
African American	270 (9.8)	5 (9.3)
Latino	154 (5.6)	2 (3.7)
Other	141 (5.1)	2 (3.7)

Abbreviations: RAPID, Researchers and Participants Interacting Directly; SKIP, Survey of Key Informants' Patients.

Figure 1. Percentage of the Total Heroin-Dependent Sample That Used Heroin or a Prescription Opioid as Their First Opioid of Abuse



Data are plotted as a function of the decade in which respondents initiated their opioid abuse.

ban or nonurban areas than in large urban areas (75.2% vs 24.8%) at the time of survey completion. The sample of abusers generally used heroin at least once a day (86.4%), had abused other substances in the past month (98.5%), and had concurrently abused prescription opioids in the 30 days prior to treatment (66.0%).

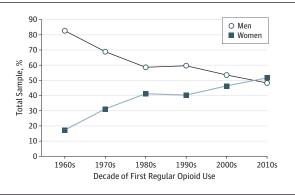
### **Opioid Abuse Initiation**

Figure 1 shows which opioids heroin users in the SKIP sample first abused, as a function of the decade in which their opioid abuse began. The number of users by decade ranged from 88 in the 1960s to more than 1600 in this century. Of those who began their opioid abuse in the 1960s, more than 80% indicated that they initiated their abuse with heroin. In a near complete reversal, 75% of those who began their opioid abuse in the 2000s reported that their first regular opioid was a prescription drug. Beginning in 2010 (2010-2013), these trajectories showed a shift in direction (ie, heroin use increased as the first opioid of abuse and prescription opioid use decreased), although the data are based on only 3 years of data collection.

## **Shifts in Demographic Characteristics**

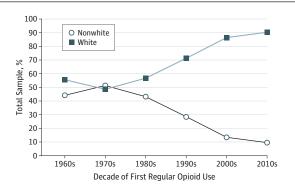
As shown in Figure 2, heroin users who started their opioid abuse in the 1960s were primarily men (82.8%). In contrast,

Figure 2. Sex Distribution of Respondents Expressed as Percentage of the Total Sample



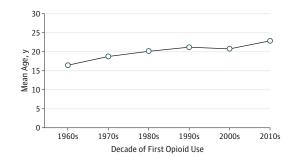
Data are plotted as a function of decade in which respondents initiated their opioid abuse.

Figure 3. Racial Distribution of Respondents Expressed as Percentage of the Total Sample of Heroin Users



Data are plotted as a function of decade in which respondents initiated their opioid abuse.

Figure 4. Mean Age of Heroin Users When They First Used an Opioid



Data are plotted as a function of the decade in which respondents initiated their opioid abuse.

the rate of women seeking treatment has increased in recent decades, such that, in our sample, by 2010, there were nearly equal numbers of male and female heroin users seeking treatment. The ethnicity of heroin users seeking treatment also showed a marked shift from nearly equal white to nonwhite

ratios in the 1960s to a dominance of white users (90.3%) by 2010 (**Figure 3**). Looking at age-related trends, as shown in **Figure 4**, we found that the mean (SEM) age of heroin users seeking treatment was 16.5 (0.3) years when they first began abusing opioids in the 1960s. The mean (SEM) age at initiation gradually increased over time to 22.9 (0.4) years in the decade starting 2010.

#### **Qualitative Studies**

Although our quantitative data suggest that some heroin users who sought treatment between 2010 and 2013 began their opioid abuse with heroin, most, particularly the vast majority of those who started their abuse after 1990, did so with prescription opioids (Figure 1). Given this strong association and the contemporary epidemic of prescription opioid abuse, the RAPID interview was focused on those who had past or current abuse of prescription opioids but who, at the time of participating, had a primary drug of heroin (n = 54). It should be noted that every RAPID respondent who indicated heroin as their primary drug also endorsed lifetime abuse of prescription opioids.

Participants were asked to explain, in an open-ended format, why they more frequently used heroin than prescription opioids. Using codes based on thematic analyses of responses, 98.1% of participants indicated that they considered the "high" from heroin to be a determining factor in its use. A third of these heroin users (31.7%) also mentioned that ease of inhalation/injection, relative to prescription opioids that require extraction, was a practical factor in the selection of heroin as a primary drug. Finally, nearly everyone (94%) indicated that they used heroin because prescription opioids were far more expensive and harder to obtain.

As one survey respondent stated: "Heroin is cheaper and stronger than the prescription drugs listed, and the supply is typically pretty consistent. It is also much easier to use intravenously than pills and other prescriptions, which often take more complex methods to break down."

This balance of "high" vs practical issues is illustrated in those affected by the introduction of an abuse-deterrent reformulation of OxyContin. As demonstrated elsewhere, <sup>20</sup> the abuse-deterrent properties resulted in a sharp decrease in the abuse of OxyContin, particularly by those who injected or inhaled their drug. However, an unanticipated outcome was increases in the abuse of other opioids, including heroin.

As another survey respondent stated: "It [OxyContin] was getting harder and harder to get the pills that you could use in a needle, most of them would just 'gel-up.' And it was cheaper and easier to get heroine [sic], which was much stronger and would get you higher than Oxycodone."

An important finding, not unrelated, was that nearly half of the respondents (48.5%) who indicated a primary drug of heroin actually preferred prescription opioids when presented with a hypothetical world where there were no limiting factors to what drug they could have. These individuals described the high of prescription opioids as "cleaner," but they used heroin instead because it was "cheaper" and "easier to find," even though its use presented legal problems not asso-

ciated with prescription opioids. These complex relationships are best illustrated by a representative quote from one of our RAPID participants: "Started using and abusing oxycondone [sic] and changed to heroin because of the price. Heroin is much cheaper than 30 mg pills of oxycondone [sic]. Although a person can still overdose it [oxycodone] is much safer and cleaner than heroin. It is legal with a prescription and wouldn't have to worry about the consequences of getting caught and the legal troubles that getting caught would cause."

In addition, our qualitative data suggest that heroin use has become common in populations that formerly only abused prescription opioids. The following quotes not only exemplify this shift but also support our SKIP findings of demographic changes in those abusing heroin: "I knew I liked it [heroin] above all else, and once I had a drug dealer it became almost too easy to get, I had access to money because I am an upper middle class family and I also became close to my dealers, driving them around so I could get paid in drugs and just becoming super close, even if it meant sexually, so I could get the drug. The 2 dealers, and the people around them...are also middle class white kids, not even kids we were all in the age range of 25-41. It just became easy, and we weren't really looked at as being addicts because everyone thinks heroin addicts are all homeless, shady looking, dirty junkies."

## Discussion

The results of these surveys indicate significant demographic differences between heroin users entering a treatment program with a DSM-IV diagnosis of opioid dependence who began their use of opioids in recent decades and heroin users who initiated use 40 to 50 years ago. Moreover, recent users of heroin were older, white men and women currently living primarily in nonurban areas who were introduced to opioids through prescription drugs or who used heroin as a cheaper and more accessible alternative to their preferred prescription opioid (eg, OxyContin). This contrasts sharply to early studies<sup>12-19</sup> that characterized the heroin problem as an inner-city issue among minority populations. Although minority groups were predominant users in the 1960s and 1970s, nearly 90% of respondents who began use in the last decade were white. The shift in demographics of heroin users over the last 2 decades can be most readily explained by 1 or more of 3 factors: first, the rapid increase in the use and misuse of opioid prescription drugs in certain populations (ie, white middle-class men and women in less urban areas) previously not exposed to opioids led to some experimentation with heroin; second, and not unrelated, because of the high cost of preferred prescription opioids, many users in our RAPID program, as reported here and elsewhere, 13,20,24-28 resorted to the use of heroin, which is much cheaper and more accessible; and finally, it appears that heroin use is now becoming more common among current prescription opioid abusers.

An interesting aspect of our data is that the age at first opioid use has increased over the past 50 years from 16 to 23 years of age, although it must be noted that recall may be limited in those reflecting back so long ago. Nonetheless, it would ap-

pear that today's heroin users began their use at a much older age than those who began 40 to 50 years ago. The reasons for this are unclear but are likely due to the fact that prescription opioids are much more readily available to younger individuals, particularly as an initial drug of abuse, given the common belief that because prescription opioids are legal, they are considered trustworthy and predictable. 26,27

There are important limitations to our studies. In terms of our treatment-based sample, one could speculate whether or not this population is representative of those using opioids "recreationally," particularly those who had access to the Internet in order to participate in our web-based follow-up. Furthermore, many factors influence the decision to enter treatment, such as family or court pressures and financial ability, which makes the population even more selective, although it is not clear that reasons for seeking treatment have changed over the past 50 years. An additional limitation is that, although there were sufficiently large numbers of patients for each decade of initiation to draw meaningful conclusions, the distribution was heavily skewed toward more recent users, as would be expected in an aging population of this sort. However, this does lead to potential biases in terms of survival cohorts or in terms of missing data from those who have matured out of their abuse. Finally, there are potential issues of recall when discussing events that have occurred a number of years ago, some of which could be significant. Obviously, however, recall is not an issue for several of our important covariates (eg, ethnicity and sex). Nonetheless, a prospective study following a cohort over decades would minimize some of these issues, but such a study is simply not feasible and would be of limited value in addressing contemporary issues. Thus, we feel that a retrospective approach can serve a useful purpose in identifying and understanding epidemiological shifts in the abuse of heroin, as well as providing an impetus for future studies.

## Conclusions

Our surveys have shown a marked shift in the demographics of heroin users seeking treatment over the past several decades. We found that heroin use is not simply an inner-city problem among minority populations but now extends to white, middle-class people living outside of large urban areas, and these recent users exhibit the same drug use patterns as those abusing prescription opioids. In this connection, our data indicate that many heroin users transitioned from prescription opioids. The factors driving this shift may be related to the fact that heroin is cheaper and more accessible than prescription opioids, and there seems to be widespread acceptance of heroin use among those who abuse opioid products. These latter conclusions are typified by a quote from one of our interviewees, which highlights the importance of these findings for future treatment and prevention efforts: "All of my friends use heroin and I know multiple people who will sell it to me or help me find someone who has it. Also if I have money I wanna spend it on something I know will get me high. If I buy pills I might not have enough money to make sure I get high."

#### ARTICI E INFORMATION

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Study concept and design: All authors.

Acquisition, analysis, or interpretation of data:
Cicero, Ellis.

Drafting of the manuscript: Cicero, Ellis.
Critical revision of the manuscript for important
intellectual content: Cicero, Surratt, Kurtz.
Statistical analysis: All authors.
Obtained funding: Cicero.
Study supervision: Cicero.

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**Role of the Sponsor:** The funding agencies had no role in the design and conduct of the study; collection, management, analysis, or interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

#### REFERENCES

- Daly EM. With rise in young painkiller abusers, officials see more heroin overdoses. California Watch. August 15, 2012. http://californiawatch.org/healthand-welfare/rise-young-painkiller-abusers -officials-see-more-heroin-overdoses-17550. Accessed July 18, 2013.
- 2. Frosch D. Prescription drug overdoses plague New Mexico. *New York Times*. June 8, 2012. http://www.nytimes.com/2012/06/09/us/in-new-mexico-battling-prescription-drug-use-that-leads-to-overdoses.html. Accessed July 18, 2013.
- 3. Seville LR, Rappleye H. Crackdown on painkiller abuse fuels new wave of heroin addiction. *NBC News*. June 7, 2012. http://investigations.nbcnews.com/\_news/2012/06/07/12091096-crackdown-on-painkiller-abuse-fuels-new-wave-of-heroin-addiction?lite. Accessed July 18, 2013.
- 4. Seelye KQ. Heroin in New England, more abundant more deadly. *New York Times*. July 18, 2013. http://www.nytimes.com/2013/07/19/us/heroin-in-new-england-more-abundant-and-deadly.html. Accessed July 18, 2013.
- 5. Dowty D. Heroin deaths spike in Onondaga County; use spreads from city to suburbs. *The Post-Standard*. June 25, 2013. http://www.syracuse.com/news/index.ssf/2013/06/heroin\_deaths\_spike in onondag.html. Accessed July 18, 2013.
- **6**. Wykoff S. Heroin finding a new home in Md suburbs. *WBAL News*. June 26, 2013. http://www

- .wbal.com/article/100864/21/template-story /Heroin-Finding-A-New-Home-In-Md-Suburbs. Accessed July 18, 2013.
- 7. Santye L. Heroin use rising at alarming rate among teens. *The Trentonian*. July 14, 2013. http://www.trentonian.com/article/20130714/NEWS01/130719794/heroin-use-rising-at-an-alarming-rate-among-teens-. Accessed July 18, 2013.
- 8. Brown KD. Heroin abuse problems plague rural Mass. towns. *Boston Globe*. July 1, 2013. http://www.bostonglobe.com/lifestyle/health-wellness/2013/06/30/heroin/C1li7rwcJgz7MtSwKtEjUP/story.html. Accessed July 18, 2013.
- **9**. Jones CM. Heroin use and heroin use risk behaviors among nonmedical users of prescription opioid pain relievers—United States, 2002-2004 and 2008-2010. *Drug Alcohol Depend*. 2013; 132(1-2):95-100.
- 10. Substance Abuse and Mental Health Services Administration (SAMHSA). Results From the 2011 National Survey on Drug Use and Health: Summary of National Findings. Rockville, MD: SAMHSA/US Dept Health and Human Services; 2012.
- 11. Unick GJ, Rosenblum D, Mars S, Ciccarone D. Intertwined epidemics: national demographic trends in hospitalizations for heroin- and opioid-related overdoses, 1993-2009. *PLoS One*. 2013;8(2):e54496.
- **12.** Lankenau SE, Teti M, Silva K, Jackson Bloom J, Harocopos A, Treese M. Initiation into prescription opioid misuse amongst young injection drug users. *Int J Drug Policy*. 2012;23(1):37-44.
- **13**. DuPont RL. Profile of a heroin-addiction epidemic. *N Engl J Med*. 1971;285(6):320-324.
- **14**. Hughes PH, Barker NW, Crawford GA, Jaffe JH. The natural history of a heroin epidemic. *Am J Public Health*. 1972;62(7):995-1001.
- **15.** Greene MH. An epidemiologic assessment of heroin use. *Am J Public Health*. 1974;64(suppl 12):1-10.
- **16**. McGlothlin WH. Drug use and abuse. *Annu Rev Psychol*. 1975;26:45-64.
- 17. Ball JC, Chambers CD, eds. *The Epidemiology of Opiate Addiction in the United States*. Springfield, IL: Thomas: 1970
- **18**. Kozel NJ, Adams EH. Epidemiology of drug abuse: an overview. *Science*. 1986;234(4779): 970-974.
- **19**. Frank B. An overview of heroin trends in New York City: past, present and future. *Mt Sinai J Med*. 2000;67(5-6):340-346.
- 20. Substance Abuse and Mental Health Services Administration (SAMHSA). Data, outcomes, and quality. Drug Abuse Warning Network (DAWN). National estimates of drug-related emergency department visits 2004-2010—all misuse and abuse. http://samhsa.gov/data/dawn.aspx#DAWN. Accessed April 24, 2014.
- 21. Peavy KM, Banta-Green CJ, Kingston S, Hanrahan M, Merrill JO, Coffin PO. "Hooked on" prescription-type opiates prior to using heroin: results from a survey of syringe exchange clients. J Psychoactive Drugs. 2012;44(3):259-265.
- 22. Cleland CM, Rosenblum A, Fong C, Maxwell C. Age differences in heroin and prescription opioid abuse among enrollees into opioid treatment programs. Subst Abuse Treat Prev Policy. 2011;6:11.

- 23. Jones CM. Frequency of prescription pain reliever nonmedical use: 2002-2003 and 2009-2010. *Arch Intern Med.* 2012;172(16):1265-1267.
- **24**. Siegal HA, Carlson RG, Kenne DR, Swora MG. Probable relationship between opioid abuse and heroin use. *Am Fam Physician*. 2003;67(5):942-945.
- **25**. Grau LE, Dasgupta N, Harvey AP, et al. Illicit use of opioids: is OxyContin a "gateway drug"? *Am J Addict*. 2007;16(3):166-173.
- **26**. Compton WM, Volkow ND. Abuse of prescription drugs and the risk of addiction. *Drug Alcohol Depend*. 2006;83(suppl 1):S4-S7.
- 27. Daniulaityte R, Falck R, Carlson RG. "I'm not afraid of those ones just 'cause they've been prescribed": perceptions of risk among illicit users of pharmaceutical opioids. *Int J Drug Policy*. 2012;23(5): 374-384.
- **28.** Cicero TJ, Ellis MS, Surratt HL. Effect of abuse-deterrent formulation of OxyContin. *N Engl J Med*. 2012;367(2):187-189.
- **29**. Khosla N, Juon HS, Kirk GD, Astemborski J, Mehta SH. Correlates of non-medical prescription drug use among a cohort of injection drug users in Baltimore City. *Addict Behav*. 2011;36(12):1282-1287.
- **30**. Daniulaityte R, Carlson RG, Kenne DR. Initiation to pharmaceutical opioids and patterns of misuse: Preliminary qualitative findings obtained by the Ohio Substance Abuse Monitoring Network. *J Drug Issues*. 2006;36(4):787-808. doi:10.1177/002204260603600402.
- **31**. Inciardi JA, Surratt HL, Cicero TJ, Beard RA. Prescription opioid abuse and diversion in an urban community: the results of an ultrarapid assessment. *Pain Med*. 2009;10(3):537-548.
- **32.** Pollini RA, Banta-Green CJ, Cuevas-Mota J, Metzner M, Teshale E, Garfein RS. Problematic use of prescription-type opioids prior to heroin use among young heroin injectors. *Subst Abuse Rehabil*. 2011;2(1):173-180.
- **33.** Mars SG, Bourgois P, Karandinos G, Montero F, Ciccarone D. "Every 'Never' I Ever Said Came True": Transitions from opioid pills to heroin injecting. *Int J Drug Policy*. 2014;25(2):257-266.
- **34**. Ciccarone D, Unick GJ, Kraus A. Impact of South American heroin on the US heroin market 1993-2004. *Int J Drug Policy*. 2009;20(5):392-401.
- **35**. Canfield MC, Keller CE, Frydrych LM, Ashrafioun L, Purdy CH, Blondell RD. Prescription opioid use among patients seeking treatment for opioid dependence. *J Addict Med*. 2010;4(2):108-113.
- **36.** US Department of Justice, National Drug Intelligence Center. National drug threat assessment 2011. http://www.justice.gov/archive/ndic/pubs44/44849/44849p.pdf. Published August 2011. Accessed April 24, 2014.
- **37**. US Department of Justice, Drug Enforcement Administration. 2011 Heroin Domestic Monitor Program: drug intelligence report. http://www.choopersguide.com/custom/domain\_1/extra\_files/attach\_1\_262.pdf. Published March 2013. Accessed April 24, 2014.
- **38**. Cicero TJ, Dart RC, Inciardi JA, Woody GE, Schnoll S, Muñoz A. The development of a comprehensive risk-management program for prescription opioid analgesics: researched abuse, diversion and addiction-related surveillance (RADARS). *Pain Med.* 2007;8(2):157-170.